

REMARKS

A. Regarding the Amendments

Pending claims 1-8, 10-13 and 15-20 have been deleted and new claims 21-32 have been added. As added, the claims are supported by the specification and the original claims and do not add new matter. Specifically, new claims 21, 22 and 24 are supported, for example by original claim 1 and the specification at, for example, page 18, line 6 to page 19, line 11 and page 20, line 18 to page 21, line 8. New claim 25 is supported, for example, by original claim 2 and new claim 26 is supported, for example, by original claim 3. Additionally, support for new claim 27 may be found, for example, at page 16, lines 4-12. New claims 28 to 32 are identical to previously added claims 15-19. Thus, upon entry of the amendments, claims 21-32 will be pending.

B. Rejection Under 35 U.S.C. § 112

To the extent that the outstanding 112 rejection, from the Office Communication mailed August 19, 2002 (Paper No. 17) applies to the new claims, Applicants respectfully traverse the rejection under 35 U.S.C. § 112, first paragraph, as containing subject matter allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 17 that claims directed to crystallization of L-aspartic acid from a suspension cooled to between 20°C and 100°C. It is the Examiner's position that crystallization in this temperature range is not supported in the specification and that, specifically, crystallization would be unlikely to occur at temperatures higher than 50°C.

The Examiner's attention is respectfully drawn to the specification at page 19, where it is stated that:

'The fumaric acid liquid is cooled to preferably 25°C or more, more preferably 30°C or more, preferably 100°C or less, more preferably 80°C or less, most preferably 60° or less. After completion of this cooling, the liquid is preferably retained at that temperature for 1 minute to 1 hour to thereby complete the deposition of L-aspartic acid crystals.'

In the claimed invention, fumaric acid is added to an ammonium L-aspartate solution, in which L-aspartic acid and a small amount of fumaric acid dissolve by forming a pairing salt with an ammonium ion. This dissolution results in a mixture. Since the ammonium L-aspartate solution is heated to a temperature within the range of 50°C to 130°C and a shearing force is applied to the mixture in the invention of claim 1 to obtain a homogenous solution, all of the added fumaric acid is dissolved (for example, the solubility of fumaric acid is 9.8g/100ml at 100°C (JIKKEN KAGAKU BINRAN p188-189, 1990 KYORITSU SHUPPAN CO., LTD., attached hereto as Exhibit A)). In the claimed invention, the ammonium L-aspartate solution is also heated to a temperature within the range of 50°C to 130°C. As set forth above, the heating step brings the solution to a temperature of from 50°C to 130°C. Therefore, the specification teaches that the solution is then cooled from that range to the 25°C to 100°C range. It is therefore submitted that there is support in the specification for cooling a solution into the 25°C to 100°C range for crystallization of L-aspartic acid from a cooled suspension, as set forth in new claims 21, 24 and 25.

Additionally, in the Examples of the invention, L-aspartic acid crystals are shown to deposit at temperatures higher than 50°C. The Examiner's attention is respectfully drawn to Examples 3, 4, 5, 6, 8 and Comparative Example 2. In all of these Examples, a combination of decreasing pressure and dropping temperatures is used to achieve crystallization. However, crystallization begins long before the temperature drops to 50°C. It is noted that on page 38 of the specification, in example 3, it is stated that, '[i]n this course, L-aspartic crystals begin to deposit at around 83°C of the liquid temperature.' Similarly, in example 5 on page 43, it is stated that 1 kg of fumaric acid added to and dissolved in a 95°C solution, and the solution is agitated for 3 minutes, '[t]hen, L-aspartic acid crystals began to deposit.' In this example, the crystals are depositing while the solution is still at 95°C. It is noted that in many of these examples

temperatures are brought to approximately 78°C and then dropped further. However, crystallization has started by the time the solution has reached 78°C. Additional support may be found in the specification at pages 17 to 18.

It is respectfully submitted that the specification provides support for a cooling range of 25°C to 100°C and that examples are given where crystallization begins at a temperature higher than 50°C. Therefore, the claims meet the written description requirement of 35 U.S.C. §112, first paragraph.

C. Rejection Under 35 U.S.C. § 103

Additionally, Applicants traverse the outstanding rejection under 35 U.S.C. 103(a) to the extent that it may apply to new claims 21 to 32. It was alleged in Paper No. 17 that the pending claims were allegedly unpatentable over Nore et al., Brun et al., Pavia et al. and Tan et al. The Examiner stated that all previous rejections were maintained and that Applicants' arguments are not persuasive. Applicants respectfully maintain their position with regard to the arguments previously set forth and assert that the claimed invention is not obvious over this combination of references, as the combination of references does not teach or suggest all of the elements of the claimed invention.

It was alleged in Paper No. 14 and maintained in Paper No. 17 that Nore teaches a method of producing aspartic acid wherein fumaric acid is added to ammonium aspartate followed by heating and crystallization. The Examiner has alleged that the fumaric acid, when in an aqueous suspension, may potentially contain alcohol. Applicants respectfully disagree.

It is Applicants' position that the fumaric acid of the invention, when in aqueous form is in water as a solvent. Webster's Dictionary at www.webster.com defines aqueous as 'of, relating to, or resembling water; made from, with, or by water.' Therefore it is respectfully submitted that the 'aqueous form' of the claimed invention refers to fumaric acid dissolved in water. The Examiner's attention is respectfully drawn to pages 45, 49 and 50 of the specification, where the

fumaric acid in the Examples is added in slurry form. In all three of these examples, the fumaric acid is combined with water to form the slurry. No additional solvents are used to create the aqueous suspension. In both the specification and the claims, there is no requirement or even a suggestion of alcohol for the aqueous suspension of fumaric acid. Additionally, the ammonium fumarate solution in new claims 21 and 24, to which the fumaric acid is added, does not contain alcohol. In the interest of advancing prosecution, Applicants have included the language 'which consists essentially of ammonium fumarate and water' to clarify the term 'ammonium fumarate solution' in claims 21 and 24. Support for this amendment may be found in the specification, for example, at page 12, lines 2-11 and Table 3. Applicants therefore respectfully submit that the aqueous suspension of claims 21 and 24, prior to and after addition of fumaric acid, clearly does not comprise alcohol.

As previously noted, the alcohol is used in Nore to increase the solubility of fumaric acid in the ammonium fumarate mixture. However, no such alcoholic solvent is necessary in the claimed invention. Instead, the claimed invention discloses addition of fumaric acid in the form of dry crystals, moisture-containing crystals or an aqueous suspension to a heated ammonium L-aspartate solution (50 to 130°C) without using an alcoholic solvent. Where a solvent is used, it is water, as set forth in the Examples. Nore, in combination with Brun, Pavia, and Tan, do not teach or suggest a heated ammonium L-aspartate solution or use of water as a solvent for fumaric acid.

Additionally, by the use of water as a solvent instead of alcohol, the claimed invention has many advantages. With use of an alcoholic solvent, the solvent may cause the degeneration of the enzyme aspartase. In contrast, in the claimed invention, the aspartase is not inhibited nor deactivated by water. It is alleged in Paper No. 17 that because aspartase has thermostable properties, it may have stability in the presence of alcohol. Applicants do not understand this allegation. Thermostability and stability in the presence of alcohol are two completely diverse characteristics of an enzyme. In heating, vibration of a molecule increases as the temperature rises. As a result, the three dimensional structure of the enzyme breaks and activity decreases.

Alternatively, degeneration of an enzyme by alcohol is caused by a change in structure. The hydrophilic enzyme surface which is a fundamental structure of the enzyme protein and the hydrophobic portion which forms the catalytic center inside the enzyme are reversed and the hydrophobic portion is brought to the surface. Aspartase changes more remarkably due to alcohol than by heating. Additionally, the Examiner asserts that there is a 'claim designed limitation to the effect that the reaction all occurs [sic] in the same pot...' However, it is noted that there is no description of 'the same pot' in the claims of the present invention. Applicants therefore respectfully request support for the Examiner's assertion that because aspartase has thermostability, it also has stability in the presence of alcohol. *show me*

In addition, as previously set forth, there are additional aspects of the invention that Nore does not teach, either alone or in combination with Brun, Pavia, and Tan. Specifically, Nore et al. does not teach a use of water as a solvent for fumaric acid, or any solvent other than an alcoholic solvent, does not teach addition of fumaric acid to a heated ammonium L-aspartate solution, does not teach the cooling rate of the claimed invention and does not teach crystallization before filtration. It is also submitted that Nore, taken in combination with Brun, Pavia, and/or Tan, still does not teach or suggest all of the elements of the claimed invention and that the claimed invention is therefore not obvious in light of these references.

Finally, the Examiner alleges that Applicants rely on the gradual cooling process as 'the crux of the invention.' Applicants agree that the cooling period is essential to the claims of the invention and point out that that period is contained in both independent claims 21 and 24, from which all of the other claims depend. It therefore Applicants' position that this requirement is adequately set forth in both of the independent claims of the invention. It is maintained that Nore and Brun do not teach a cooling step as in the claimed invention, as set forth in Applicants' response mailed June 5, 2002.

Furthermore, the crystallization of L-aspartic acid may occur by only retaining a reaction solution for 0.1 second to 1 hour upon dissolution of the fumaric acid (see, for example,

specification page 16, lines 19-22). In this case, the crystallization of L-aspartic acid begins under high temperature conditions by this operation without cooling. Since the resultant mixture is a supersaturated solution due to addition of fumaric acid to the heated ammonium L-aspartate solution in a molar ratio of 0.4 to 0.8 to the total molar amount of ammonium L-aspartate and ammonium fumarate contained in the ammonium L-aspartate solution in the claimed invention, crystallization may occur easily at high temperature by a salt exchange reaction in order to resolve the instability of a supersaturated solution. 4

Additionally, although the crystallization of L-aspartic acid in the claimed invention occurs while cooling to 100°C, it does not mean stopping cooling at 100°C. Further cooling to a lower temperature is intended (see, for example, specification page 19, lines 12-15). }

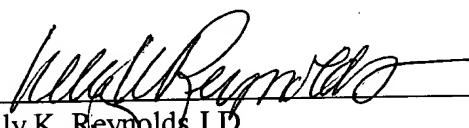
The claimed invention teaches a method of preparing aspartic acid wherein fumaric acid is dissolved in the heated ammonium L-aspartate solution and L-aspartate is crystallized under specific conditions without an alcoholic solvent, which is not taught or suggested by the cited references. Additionally, the method of the present invention can successfully produce a needle-like L-aspartic acid crystal having mainly 30-1000 μm (see, for example, specification page 19, lines 18-19). Therefore, in filtration of needle-like L-aspartic crystals of this size, liquid passes through them quickly. Thus, their purity can be improved by simple washing operations. This effect cannot be obtained in any of the cited references, nor was it taught or suggested by the cited references. As Nore et al., viewed in light of Brun et al., Pavia et al. and Tan et al. do not teach or suggest all of the elements of the claimed invention, claims 21-32 are not obvious in light of those references.

CONCLUSION

Enclosed is a check in the total amount of \$860.00, which includes \$110.00 for the One (1) Month extension of time fee and \$750.00 for the filing of an RCE application. Please charge Deposit Account No. 50-1355 the amount of \$280.00 for the multiple dependent claim fee and any other fees or credits believed to be due. A copy of the Transmittal Sheet is enclosed. The Examiner is invited to contact Applicants' undersigned representative if there are any questions related to this matter.

Respectfully submitted,

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